Chronic Pain and Psychiatric Comorbidities in Fibromyalgia and Temporomandibular Disorders: A Systematic Review

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University of Rochester School of Medicine and Dentistry
Communications Director
ACTTION
Affiliations and Disclosures

- Financial support for this project was provided by ACTTION, a public-private partnership, which has received research contracts, grants, or other revenue from FDA, multiple pharmaceutical and device companies, and other sources.

- Previously employed by, PinneyAssociates (2014-2018), a consulting firm that provides scientific and regulatory advice to pharmaceutical industry (risk management, abuse liability OTC switch) and tobacco companies (vapor products only/harm reduction).
Background – Index Disorders

- **Fibromyalgia (FM)**
  - Musculoskeletal pain disorder often including widespread muscle pain and tenderness
    - **Diagnosis**: American College of Rheumatology (ACR; Wolfe et al., 2011; Arnold et al., 2019)
    - **Prevalence**: 0.2 to >11% (estimates can vary considerably; Marques et al., 2017)
    - Gender differences (Wolfe et al., 2018)

- **Temporomandibular Disorders (TMD)**
  - Orofacial pain disorder involving the temporomandibular joint
    - **Diagnosis**: Research Diagnostic Criteria (RD; Schiffman et al., 2014)
    - **Prevalence**: 5 to 12% (NIH, 2019)
Background – Index Disorders and Central Sensitization

Centralised Sensitisation

Assessment and manifestations of central sensitisation

- Pelvic pain/interstitial cystitis
- Endometriosis
- Postoperative chronic pain
- Vulvodynia
- Chronic Pancreatitis
- IBS
- Non-cardiac chest pain
- TTH/CTTH
- Migraine
- TMD
- Myofascial pain syndrome
- Shoulder impingement syndrome

- Primary dysmenorrhea
- Chronic fatigue syndrome
- Restless legs
- Post traumatic stress disorder
- Whiplash
- Fibromyalgia
- Osteoarthritis
- Rheumatoid arthritis
- Neurogenic pain
- CLPB
- Multiple chemical sensitivity
Background – Comorbid Disorders

- FM and TMD are overlapping conditions that share many key symptoms (generalized pain, bowel complaints, headache; Aaron et al., 2000; Plesh et al., 1996)

- Why examine comorbidities?
  - Better understand the patient experience:
    - patient symptoms and pain perception
    - disability and reduce quality of life
  - Inform diagnosis of index disorder (e.g., FM or TMD)
  - Examine shared etiological pathways across conditions
  - Refine treatment approach
Objectives

- Provide overview of published literature examining chronic pain and psychiatric comorbidities in FM and TMD
- Determine the incidence and/or prevalence of these comorbidities in FM and TMD
Methods

- **Systematic Review Search Strategy**
  - PROSPERO registration #CRD42019133249
    - Search terms: (fibromyalgia or temporomandibular disorders) AND (comorbidity or comorbid) AND (incidence or prevalence or cross-sectional or cohort) AND (psychiatric or mental health disorder or chronic pain)

- **Inclusion criteria**
  - Criteria-based diagnosis of FM (ACR) and TMD (DC)
  - Psychiatric outcomes – Mood, Anxiety, Personality disorders diagnosed via structured interview using a standardized assessment tool (Løge-Hagen et al., 2019)
Records identified through database searching:
- Pubmed = 471
- Embase = 281
- PsychInfo = 54
- Total n = 806

Additional records identified through other sources:
- n = 49

Records after duplicates removed:
- n = 683

Records screened:
- n = 683

Records excluded:
- n = 514

Full-text articles assessed for eligibility:
- n = 169

Full-text articles excluded, with reasons:
- n = 125

Studies included in qualitative synthesis:
- n = 44
  - including 6 overlapping studies

Final Study count:
- n = 41
  - including 2 studies that had data for both FM and TMD
Excluded Studies (N = 125)

- Diagnostic criteria did not meet standards (75% of studies excluded: 95 studies)
  - Self-report of psychiatric disorders (47 studies)
  - FM not diagnosed with ACR criteria (33 studies)
  - TMD not diagnosed with RDC criteria (15 studies)
- Prevalence/incidence of chronic Pain/Psychiatric disorders not assessed (15 studies)
- Not a research study/not English/FM or TMD not assessed (14 studies)
- TMD diagnosis acute only (1 study; Lorduy et al., 2013)
Overview of Studies (N = 41)

- **Study design**: cross-sectional
  - Some studies were cohort studies that compared the index disorder group to a control, non-FM/TMD group
  - Only cross-sectional data were included from FM/TMD group

- **Publication years**
  - 1992 to 2018

- **Study locations**
  - US (14)
  - Italy (10)
  - Brazil (4)
  - Turkey (4)
  - Other countries: Canada, Germany, Israel, Norway, Saudi Arabia, Spain, and Sweden
Overview of Study Participants

- Participants were recruited from outpatient clinic settings (convenience sampling – a subset were consecutive sampling)

- Sample size
  - 22 to 77,087 (median = 100)

- Mean participant age
  - Adults 33 to 58 years (median = 47.2)

- Gender
  - 40/41 studies women were majority
  - Nearly half of studies included only women (n=18)

- Disease duration
  - 3.9 to 11.43 years (median = 7.72)
### Overview of Results

<table>
<thead>
<tr>
<th>Index Disorder</th>
<th>Chronic Pain (22 studies)</th>
<th>Psychiatric (25 studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FM (37 studies)</td>
<td>13 studies</td>
<td>24 studies</td>
</tr>
<tr>
<td>TMD (10 studies)</td>
<td>9 studies</td>
<td>1 study</td>
</tr>
</tbody>
</table>

Study counts across cells do not total 41 due to overlapping study data sets (6 studies) and the inclusion of both FM and TMD patients in 2 studies (Aaron et al., 2000; Plesh et al., 1996).
## FM and Chronic Pain Comorbidities

<table>
<thead>
<tr>
<th>Index Disorder</th>
<th>Comorbid Disorder</th>
<th>Chronic Pain</th>
<th>Psychiatric</th>
</tr>
</thead>
<tbody>
<tr>
<td>FM</td>
<td>13 studies</td>
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<tr>
<td>TMD</td>
<td>9 studies</td>
<td></td>
<td>1 study</td>
</tr>
</tbody>
</table>
FM and Chronic Pain

**Lifetime Prevalence (4 studies)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage (%)</th>
<th>Values at the end of each bar represent the number of patients that had the corresponding comorbidity in each study.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache (migraine)</td>
<td>18</td>
<td>102</td>
</tr>
<tr>
<td>Headache (chronic tension-type)</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Irritable Bowel Syndrome</td>
<td>17</td>
<td>208</td>
</tr>
<tr>
<td>Genital</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>Interstitial Cystitis</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Lower Back</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>TMD</td>
<td>102</td>
<td>2</td>
</tr>
</tbody>
</table>

Each bar represents a prevalence estimate (%) from an individual study.
FM and Chronic Pain

**Current Prevalence (10 studies)**

- Analgesic overuse: 6%
- Trauma-related: 4%
- Migraine: 32%, 15%
- Tension: 18%, 16%
- Migraine + Tension: 21%, 8%
- Irritable Bowel Syndrome: 232%, 13%
- Pelvic: 8%
- Interstitial Cystitis: 128%
- Rheumatoid Arthritis: 30%
- TMD: 45%, 330%

Percentage (%)

Percentage (%)
## TMD and Chronic Pain Comorbidities

<table>
<thead>
<tr>
<th>Index Disorder</th>
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<th>Psychiatric</th>
</tr>
</thead>
<tbody>
<tr>
<td>FM</td>
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</tr>
</tbody>
</table>
TMD and Chronic Pain

**Lifetime Prevalence (2 studies)**

- **Headache (chronic tension-type)**: 9%
- **IBS**: 167%
- **Genital/Pelvic**: 2%
- **Lower Back**: 4%
- **Rheumatoid Arthritis**: 46%
- **FM**: 90%

Percentage (%)
TMD and Chronic Pain

Current Prevalence (7 studies)

- Myofascial Syndrome: 21%
- Migraine: 87%
- Headache (general): 97%
- Irritable Bowel Syndrome: 16%
- Stomach (general): 51%
- Genital/Pelvic: 11%
- Back (general): 61%
- Chest (general): 33%
- Osteoarthritis: 10%
- FM: 7%
## FM and Psychiatric Comorbidities

<table>
<thead>
<tr>
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</thead>
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<tr>
<td>TMD</td>
<td>9 studies</td>
<td>1 study</td>
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</tbody>
</table>
### FM and Anxiety Disorders

**Lifetime Prevalence (10 studies)**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agoraphobia</td>
<td>15</td>
</tr>
<tr>
<td>Phobia (Social)</td>
<td>16</td>
</tr>
<tr>
<td>Phobia (Specific)</td>
<td>17</td>
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<tr>
<td>Phobia (General)</td>
<td>12</td>
</tr>
<tr>
<td>Obsessive Compulsive Disorder</td>
<td>5</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>17</td>
</tr>
<tr>
<td>PTSD</td>
<td>54</td>
</tr>
<tr>
<td>Generalized Anxiety Disorder</td>
<td>12</td>
</tr>
</tbody>
</table>

**Disorders**
- Agoraphobia
- Phobia (Social)
- Phobia (Specific)
- Phobia (General)
- Obsessive Compulsive Disorder
- Panic Disorder
- PTSD
- Generalized Anxiety Disorder

**Percentage (%)**

<table>
<thead>
<tr>
<th>0</th>
<th>10</th>
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</tbody>
</table>
FM and Anxiety Disorders

Current Prevalence (16 studies)

- Agoraphobia: 2%
- Phobia (Social): 4%
- Phobia (Specific): 14%
- Phobia (General): 10%
- Obsessive Compulsive Disorder: 0%
- Panic Disorder: 7%
- Phobia (Social): 5%
- Phobia (Specific): 8%
- Phobia (General): 16%
- Phobia (Specific): 7%
- Phobia (General): 9%
- PTSD: 2%
- General Anxiety Disorder: 10%
- Anxiety (general): 11%
- Anxiety (general): 33%
- Anxiety (general): 15
- Anxiety (general): 179
- Anxiety (general): 20,103
- Anxiety (general): 44
- Anxiety (general): 15,858
- Anxiety (general): 85
- Anxiety (general): 9
- Anxiety (general): 27

Percentage (%)
FM and Mood Disorders

**Lifetime Prevalence (15 studies)**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bipolar Disorder</td>
<td>2, 6, 15</td>
</tr>
<tr>
<td>Major Depressive Disorder</td>
<td>10, 19, 50</td>
</tr>
<tr>
<td>Depression (general)</td>
<td>20, 31, 60</td>
</tr>
<tr>
<td>Dysthymic Disorder</td>
<td>1, 259, 58</td>
</tr>
</tbody>
</table>

**Legend:**
- 1: 0-10%
- 2: 10-20%
- 3: 20-30%
- 4: 30-40%
- 5: 40-50%
- 6: 50-60%
- 7: 60-70%
- 8: 70-80%
- 9: 80-90%
- 10: 90-100%
FM and Mood Disorders

Current Prevalence (15 studies)

- **Bipolar Disorder**: 1(2) 5(9) 3827(77)
- **Major Depressive Disorder**: 6(17) 17(53) 88(23) 12,889
- **Depression (general)**: 5(28) 28(145) 26,896
- **Mood disorder (general)**: 23(11) 12(12)
### TMD and Psychiatric Comorbidities

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<tr>
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</table>

- **Chronic Pain**: TMD (9 studies), FM (13 studies)
- **Psychiatric**: TMD (1 study), FM (24 studies)
TMD and Psychiatric Disorders - Prevalence 1 study

- Nifosi et al., 2007 (N=63) assessed current psychiatric comorbidities:
  - GAD – 9.5% (n=6)
  - MDD – 17.5% (n=11)
  - Panic Disorder – 6.3% (n=4)
Summary of Findings

- All 41 studies cross-sectional and included adult patients from outpatient clinics
- Most included women in middle-age and focused on FM (n=37) rather than TMD (n=10)

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>FM</td>
<td>TMD</td>
</tr>
<tr>
<td>TMD</td>
<td>Headache Disorders</td>
</tr>
</tbody>
</table>

Listed comorbidities included prevalence estimates >30% in at least 2 reviewed studies
Limitations

- Small (41) number studies on prevalence (none on incidence).
- Potential for selection bias (sample size 100 or less for most studies, patients recruited through convenience sampling)
  - Methodological trade-off: large sample, population-based studies with less specific diagnostic criteria not included
- All or majority of studies focused on women and FM
  - Women tend to report more health symptoms
  - Number of men diagnosed with FM might be higher than previously thought (Wolfe et al., 2018)
- Shifting prevalence rates over time due to evolving diagnostic criteria over last ~30 years (see Arnold et al., 2019)?
Additional Considerations

- Juvenile FM (Yunus and Masi criteria; Ting et al., 2016)
- Temporal order of co-occurring index and comorbid conditions
- Known relationships between comorbidities (e.g., anxiety and depression; Valtri et al., 2012)
- Sleep-related comorbidities
  - Sleep issues a key symptom of FM (Arnold et al., 2019)
  - Two systematic reviews have examined sleep quality and FM or TMD (Keskindag & Karaaziz, 2017; Veiga et al., 2013)
Special thanks to to my invaluable co-reviewers!

Dr. McKenzie Ferguson  
(Southern Illinois University Edwardsville  
School of Pharmacy)

Dr. Ewan McNicol  
(Pharmacy Practice, MCPHS University)
<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>Sample size</th>
<th>Dates of data collection</th>
<th>First author</th>
<th>Year</th>
<th>Sample size</th>
<th>Dates of data collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aaron</td>
<td>2000 (TMD)</td>
<td>25</td>
<td>Jan 1993-Sept 1994</td>
<td>Genc</td>
<td>2011</td>
<td>50</td>
<td>NR</td>
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<tr>
<td>Al-Harthy</td>
<td>2017</td>
<td>122</td>
<td>NR</td>
<td>Gündüz</td>
<td>2018</td>
<td>52</td>
<td>Feb 2014-May 2014</td>
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<td>Alciati</td>
<td>2016</td>
<td>75</td>
<td>May 2010-2011</td>
<td>Hudson</td>
<td>1992</td>
<td>33</td>
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<td>Bazzichi</td>
<td>2010</td>
<td>314</td>
<td>NR</td>
<td>Marcus</td>
<td>2005</td>
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<td>Bernatsky</td>
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<td>NR</td>
<td>Nifosi</td>
<td>2007</td>
<td>63</td>
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<tr>
<td>Brooks</td>
<td>2015</td>
<td>219</td>
<td>2009-2010 (months NR)</td>
<td>Plesh (FM)</td>
<td>1996</td>
<td>60</td>
<td>NR</td>
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<tr>
<td>Carta</td>
<td>2006</td>
<td>37</td>
<td>NR</td>
<td>Rodriguez</td>
<td>2015</td>
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<td>NR</td>
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<td>71</td>
<td>March 2015-July 2015</td>
<td>Rodriguez</td>
<td>2015</td>
<td>536</td>
<td>NR</td>
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<td>77</td>
<td>NR</td>
<td>Ross</td>
<td>2010</td>
<td>76</td>
<td>NR</td>
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<td>Consoli</td>
<td>2012</td>
<td>167</td>
<td>NR</td>
<td>Thieme</td>
<td>2004</td>
<td>115</td>
<td>NR</td>
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<tr>
<td>Dahan</td>
<td>2016</td>
<td>180</td>
<td>NR</td>
<td>Uguz</td>
<td>2010</td>
<td>103</td>
<td>NR</td>
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